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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,098	04/28/2006	Taro Miyazaki	14875-154US1 C1-A0304P-US	1173

26161 7590 07/13/2007

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EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	

MAIL DATE	DELIVERY MODE
07/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,098	MIYAZAKI ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-21 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-21 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-21 are all the pending claims subject to lack of unity restriction.

Lack of Unity: Restriction

2. Restriction is required under 35 U.S.C. 121 and 372.

In assessing whether the requirements of unity of invention of an application are met, identification of the technical features that each solution to a technical problem contributes over the prior art (special technical features) must be made. If then a technical relationship between the solutions, involving one or more of the same technical features, can be recognized, the requirements of unity of invention are said to be met.

3. The invention in Claims 1-21 does not involve an inventive step in light of the following references:

Carter et al., J. Immunol. Methods 248:7-15 (2001); cited in the IPER filed 12/9/05 and IDS of 4/28/06;

Ridgeway et al., Protein Eng. 9:617-612 (1996); cited in the IPER filed 12/9/05 and IDS of 4/28/06;

Peipp et al., Biochem. Soc. Trans. 30:507-511 (2002); cited in the IPER filed 12/9/05 and IDS of 4/28/06;

Shalaby et al., J. Exp. Med. 175:217-225 (1992); cited in the IPER filed 12/9/05 and IDS of 4/28/06.

Carter and Ridgeway describe a process for producing a bispecific antibody having an Fc region, wherein the H chain and L chain which constitute a first set disclosed in this application having a particular antigen recognition site and the H chain and L chain which constitute a second pair disclosed in this application having antother antigen recognition site are expressed simultaneously, and the formation of the first pair and the second pair and the bonding of said first pair and second pair by knobs-in-hole are carried out simultaneously. Carter and Ridgeway also describe antibodies produced having antigen recognition sites comprising undesirable sets comprising the H chain which makes up the first pair and the L chain which makes up the second pair. In addition, Carter, Peipp and Shalaby describe the V region of the H chain and L chain which constitute a particular antigen recognition site and the V region of H chain and L chain which make up another antigen recognition site are separately expressed in E coli and that the respective H chain and L chain are bonded in advance and their respective antigen recognition sites formed, after which the two antigen recognition sites are chemically bonded, thereby efficiently producing the target bispecific antibody.

The process for producing a bispecific antibody having an Fc region described in Carter and Ridgeway could readily have been modified by one of skill in the art based on Carter, Peipp and Shalaby disclosing that the separate expression of an H chain and L chain which constitute a first pair having a particular antigen recognition site and a H chain and L chain which constitute a second pair having another antigen recognition site, and to bond their respective H chain and L chains in advance, forming a first pair and a second pair having antigen recognition site, and subsequently bonding the first

pair and second pair via knob-in-hole, in order to prevent the production of antibodies having antigen recognition sites comprising undesirable sets and to efficiently produce the target bispecific antibody. Further one of skill in the art could introduce an optimum expression regulating factor and carry out the expression of the H chain and L chain which constitute the first pair and H chain and L chain which constitute the second pair in separate cells at different times. Further one of skill in the art could use the production process to produce a bispecific antibody and a composition containing the antibody to produce a cell having the vector introduced and to produce a kit containing the vector.

Although the claims are common to each other in relating to an antibody comprising a heavy chain and a light chain, the subject matter was publicly known and therefore the common matter is not a special technical feature within the meaning of PCT 13.2.

4. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. The resulting separate inventions, as presently identified, have been grouped according to the order in which they have been claimed.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1, 2, 5-8, drawn to a method for producing an antibody comprising a first pair and a second pair, the contact of the first light chain not bonded to the first heavy chain with the second heavy chain not bonded to the second light

chain, and the contact of the first heavy chain not bonded to the first light chain with the second light chain not bonded to the second heavy chain.

Group II, claim(s) 3-8, drawn to a method for producing an antibody comprising the step of forming a first pair, the step of forming a second pair and the step of forming the antibody with the use of the first and second pairs.

Group III, claim(s) 9, 17-20, drawn to a method for expressing an antibody from a first vector for expressing the first heavy chain and the first light chain induced by a first expression regulatory factor and a second vector expressing a second heavy chain and the second light chain is induced by a second expression regulatory factor, a vector for expressing a light chain and a heavy chain, and a cell comprising a vector, and a cell capable of expressing a first and second pair of an antibody.

Group IV, claim(s) 10-13, drawn to a method for increasing the proportion or production of an antibody composition comprising expressing a first and second antibody at different times, a method of suppressing the production of antibodies other than a first pair and a second pair at different times, and a method of expressing a first and second antibody pair at different times with distinct expression inducing agents.

Group V, claim(s) 14-16 and 21, drawn to an antibody composition having an antibody containing the first pair and the second pair at a high ratio.

5. As no technical features can be distinguished which, in light of the prior art, could be regarded as special technical features on which a unifying concept could be based, there is no single inventive concept underlying the plurality of claimed inventions.

6. The methods of Groups I-IV differ in the method objectives, method steps and parameters and in the reagents used. The method of Group I requires producing a bispecific antibody into which knobs-in-hole has been introduced where the process requires a step of preparing a first pair and a step of preparing a second pair and step of preparing antibodies using the first and second pair; the method of Group II requires producing an antibody containing steps a, b, and c regardless of the order and is

understood to include a process where the three steps are carried out simultaneously; the method of Group III requires an expression vector for expressing a first light and heavy chain and a second vector for expressing a second light and heavy chain; and the method of Group IV requires increasing the production of an antibody composition by expressing a first pair and a second pair of antibodies at different timings or suppressing the expression of other antibodies than a first and a second pair. Thus the inventions of Groups I-IV are separate and distinct in having different method steps and different endpoints and are patentably distinct.

7. Inventions of Group V and Groups I-IV are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the antibody can be produced by synthetic methods. AS for the method, a materially different product could be produced such as a fusion protein comprising two different cytokines or growth factors.

8. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product

are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

9. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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